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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/585,693	11/09/2006	Takashi Yamashita	Q95455	4348

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EXAMINER	
WILSON, MICHAEL C	
ART UNIT	PAPER NUMBER
1632	

NOTIFICATION DATE	DELIVERY MODE
04/28/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/585,693	YAMASHITA ET AL.	
	Examiner	Art Unit	
	MICHAEL WILSON	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 February 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,5-23 and 28-31* is/are pending in the application.

4a) Of the above claim(s) *7-23 and 28-30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,5,6 and 31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's arguments filed 2-15-11 have been fully considered but they are not persuasive.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 2, 4 and 24-27 have been canceled. Claim 31 has been added. Claims 1, 3, 5-23, 28-31 are pending.

Election/Restrictions

This application contains claims 7-23, and 28-30, drawn to an invention nonelected with traverse in the reply filed on 12-28-07. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claims 1, 3, 5, 6 are under consideration.

Claim Objections

The objection regarding the first step of the product-by-process claim 1 has been withdrawn in view of the amendment.

The objection of claim 1 regarding the grammar of the "microinjecting" step has been withdrawn in view of the amendment.

The phrase "wherein the microinjection" in claim 1 is objected to because the antecedent term is "microinjecting"; therefore, the phrase would be more clear written as –wherein the microinjecting--. Likewise, "the incubation" at the end of claim 1 should clearly refer to –the incubating--.

Claim Rejections - 35 USC § 112

Indefiniteness

Claims 1, 3, 5, 6 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The rejection regarding the phrase "the early embryo thereof" in claim 1 has been withdrawn in view of the amendment.

The rejection of claim 1 regarding the phrase "at a stage except for and after the blastodermic stage just after egg laying... ...wherein the early embryo is at least 24 after the start of incubation" has been withdrawn because the phrase has been deleted.

Claim Rejections - 35 USC § 102

The rejection of claims 1, 3, 5, and 6 under 35 U.S.C. 102(b) as being anticipated by Harvey (Nature Biotechnology, April 2002, Vol. 19, pg 396-399) has been withdrawn because Harvey did not teach a retroviral vector encoding an antibody now required in claim 1 (incorporated from claim 4 which is now canceled).

The rejection of claims 1, 3, 5, and 6 under 35 U.S.C. 102(a) as being anticipated by Rapp (Transgenic Res., Oct. 2003, Vol. 12, pg 569-575) as supported by Speksnijder (2000, Poultry Sci., Vol. 79, pg 1430-1433) has been withdrawn because Rapp did not teach a retroviral vector encoding an antibody now required in claim 1 (incorporated from claim 4 which is now canceled).

Claims 1, 3, 5, 6 remain rejected under 35 U.S.C. 102(e) as being anticipated by MacArthur (US Patent 6,825,396).

MacArthur taught a transgenic chicken comprising a transgene encoding interferon alpha or erythropoietin (claim 1). The chickens described by MacArthur were made using a REV vector comprising an ovalbumin promoter and a lysozyme signal sequence (Fig. 2; claim 1). MacArthur also taught the vector could encode antibodies, factor VIII, G-CSF, and immunoreactive proteins (i.e. immunotoxins) et al. (col. 4, lines 36-55). The retrovirus was injected into freshly laid egg embryos (Stage X; col. 14, line 60-65).

The phrase "wherein the microinjection occurs at least 24 hours after the start of incubation" in claim 1 does not distinguish the structure of the transgenic chicken claimed or made by applicants from the transgenic chicken described by MacArthur. Therefore, the transgenic chicken described by MacArthur has the same structure as a transgenic chicken injected at Stage XI, 24 hours after the start of incubation (claim 1), or 48 hours after the start of incubation (claim 3) as claimed and has the same structure as the transgenic chicken disclosed by applicants.

The chicken of MacArthur inherently has the "antibody content not lower than 5 µg/ml in egg white, 1 µg/ml in egg white, or 1 µg/ml in egg yolk" as in claim 1 as amended because it has the same structure described by applicants as being part of the invention. The transgenic chicken injected at Stage X and bred to G1 described by MacArthur inherently expresses the amount of protein claimed because it has the same structure as a transgenic chicken microinjected at least 24 hours after the start of

incubation (Stage XI?) and bred to G1 as claimed. Furthermore, expression is also affected by positional effects upon integration of the retroviral vector, the amount of retroviral vector microinjected, and time; therefore, the amounts of expression claimed are well within the expression levels obtained using the method described by MacArthur.

Claim 6 has been included because MacArthur taught G2 chickens, which inherently have the same structure as the G2 chickens disclosed by applicants and encompassed by claim 6.

Response to arguments

Applicants argue Macarthur only exemplified making chickens encoding β-gal; therefore, applicants conclude MacArthur does not anticipate making chickens encoding antibodies as claimed. Applicants' argument is not persuasive. MacArthur is not limited to chickens encoding β-gal; MacArthur taught the chickens could encode antibodies (col. 4, lines 36-55).

Applicants' argue administration of the vector at Stage X results in transgene silencing – whereas the method claimed does not. Applicants' argue the method of MacArthur did not teach the amount of expression claimed. Applicants' argument is not persuasive. Applicants' discussion of gene silencing as it relates to Harvey (pg 13 of the response filed 2-15-11) must be put into context of MacArthur. Applicants' discussion under Harvey is not persuasive. The structure of the transgenic chicken injected at Stage X and bred to G1 described by MacArthur expresses the amount of

expression obtained when the transgenic chicken is injected at least 24 hours after the start of incubation (Stage XI?) and bred to G1 as claimed. Tables 1-4 do not teach otherwise. Furthermore, expression is also affected by positional effects upon integration of the retroviral vector, the amount of retroviral vector microinjected, and time; therefore, it is not readily apparent that the amounts of expression obtained by applicants are out of reach using the method described by MacArthur.

Claims 1, 3, 5, 6 remain rejected under 35 U.S.C. 102(e) as being anticipated by Ivarie (US Patent 6,730,822).

Ivarie taught a G1 transgenic chicken comprising a transgene encoding an exogenous protein (col. 25, line 30). The chickens described by Ivarie were made using replication-defective retrovirus (col. 19, line 52) and could encode antibodies (col. 19, line 39). The retrovirus was injected into early egg embryos (Stage VII-XII; col. 11, line 38).

The phrase "wherein the microinjection occurs at least 24 hours after the start of incubation" in claim 1 is met by Ivarie who taught microinjecting at Stage XII (col. 11, line 38) which is at least 24 hours after the start of incubation. Furthermore, the phrase does not distinguish the structure of the transgenic chicken claimed or made by applicants from the transgenic chicken made by microinjecting at Stage VII-XI described by Ivarie. Therefore, the transgenic chicken described by Ivarie has the same structure as a transgenic chicken injected at least 24 hours after the start of incubation (claim 1),

or 48 hours after the start of incubation (claim 3) as claimed and has the same structure as the transgenic chicken disclosed by applicants.

The chicken of Ivarie inherently has the "antibody content not lower than 5 μg/ml in egg white, 1 μg/ml in egg white, or 1 μg/ml in egg yolk" as in claim 1 as amended because it was made using the method claimed (microinjecting at least 24 hours after the start of incubation) and has the same structure described by applicants as being part of the invention. In addition, the transgenic chicken injected at Stage VII-XI and bred to G1 described by Ivarie inherently expresses the amount of protein claimed because it has the same structure as a transgenic chicken microinjected at Stage XII and bred to G1 as claimed. Furthermore, expression is also affected by positional effects upon integration of the retroviral vector, the amount of retroviral vector microinjected, and time; therefore, the amounts of expression claimed are well within the expression levels obtained when microinjecting at Stage VII-XI described by Ivarie.

Claim 6 has been included because Ivarie taught G2 chickens, which inherently have the same structure as the G2 chickens disclosed by applicants and encompassed by claim 6.

Response to arguments

Applicants argue Ivarie only exemplified making chickens encoding β-gal; therefore, applicants conclude Ivarie does not anticipate making chickens encoding antibodies as claimed. Applicants' argument is not persuasive. Ivarie is not limited to

chickens encoding β-gal; Ivarie taught the chickens could encode antibodies (col. 19, line 39).

Applicants' argue the method of Ivarie did not teach the amount of expression claimed. Applicants' argument is not persuasive. Ivarie taught all the method steps claimed including encoding an antibody and microinjecting at Stage XII (which is at least 24 hours after the start of incubation as claimed); therefore, the method inherently results in the amount of expression claimed. Applicants' discussion of gene silencing as it relates to Harvey (pg 13 of the response filed 2-15-11) must be put into context of Ivarie and microinjection at Stage VII-XII. More importantly, the transgenic chicken injected at Stage VII-XII and bred to G1 described by Ivarie inherently expresses the amount of protein claimed because it has the same structure as a transgenic chicken microinjected at least 24 hours after the start of incubation (Stage XI?) and bred to G1 as claimed. Tables 1-4 do not teach otherwise. Furthermore, expression is also affected by positional effects upon integration of the retroviral vector, the amount of retroviral vector microinjected, and time; therefore, it is not readily apparent that the amounts of expression obtained by applicants are out of reach using the method described by Ivarie.

Claims 1, 3, 5, 6 remain rejected under 35 U.S.C. 102(e) as being unpatentable over Sang (U.S. Patent Application Publication 2005/0273872), as evidenced by Kamachi (Development 125:2521-2532; 1998).

Sang taught transgenic avians and the expression of transgene encoded protein within the avian egg (Title and Abstract). Replication defective vectors, such as ALV and other lentiviruses are taught in paragraph [0013], on p. 2 and paragraph [0017], p. 3. Lentiviruses are described as a subgroup of the retroviruses (paragraph [0015], p. 3). Sang specifically taught obtaining fertile hen's eggs containing developing chick embryos at developmental stages X-XIII ; and injection of VSV-G pseudotyped lentiviral vector into the subgerminal cavity below the embryo (Experiment 1, paragraph [0064], p. 5), to produce G0 transgenic chickens (paragraph [0090], p. 7). Stage 13 chick embryos include the gastrula stage, i.e. up to and including 48 hours; such is evidenced by Kamachi in describing the expression of the lens-specific crystallin gene in the developing chicken (first column, under summary; limitation of claims 1 and 3). Germ line transmission from G0 males and breeding by crossing to stock hens and screening their G1 offspring is described in paragraph [0092], p. 7. The analysis of G1 transgenic birds and transmission to G2 from the founder birds is described in paragraphs [0093-0095], p. 7 (limitation of claim 6). Transgene expression in G1 and G2 transgenic birds is taught in paragraph [0096], pp. 7-8. Sang taught the transgene material may encode any of a large number of proteins, and may include sequences encoding antibodies (paragraph [0030], p. 4; limitation of claim 4).

The transgenic chicken made by injecting stage X-XIII embryos is a transgenic chicken injected at least 24 hours after the start of incubation (claim 1), or 48 hours after the start of incubation (claim 3) as claimed and has the same structure as the transgenic chicken disclosed by applicants.

Accordingly, the chicken of Sang inherently has the "antibody content not lower than 5 µg/ml in egg white, 1 µg/ml in egg white, or 1 µg/ml in egg yolk" as in claim 1 as amended because it was made using the method claimed (microinjecting at least 24 hours after the start of incubation) and has the same structure described by applicants as being part of the invention. In addition, the transgenic chicken injected at Stage X-XIII and bred to G1 described by Sang inherently expresses the amount of protein claimed because it has the same structure as a transgenic chicken microinjected and bred to G1 as claimed.

Claim 6 has been included because Ivarie taught G2 chickens, which inherently have the same structure as the G2 chickens disclosed by applicants and encompassed by claim 6.

Response to arguments

Applicants argue Sang only exemplified making chickens encoding β-gal; therefore, applicants conclude Sang does not anticipate making chickens encoding antibodies as claimed. Applicants' argument is not persuasive. Sang is not limited to chickens encoding β-gal; Sang taught the chickens could encode antibodies.

Applicants' argue the method of Sang did not teach the amount of expression claimed. Applicants' argument is not persuasive. Sang taught all the method steps claimed including encoding an antibody and microinjecting at Stage XII (which is at least 24 hours after the start of incubation as claimed); therefore, the method inherently results in the amount of expression claimed. Applicants' discussion of gene silencing as

it relates to Harvey (pg 13 of the response filed 2-15-11) must be put into context of Sang and microinjection at Stage VII-XII. More importantly, the transgenic chicken injected at Stage VII-XII and bred to G1 described by Sang inherently expresses the amount of protein claimed because it has the same structure as a transgenic chicken microinjected at least 24 hours after the start of incubation (Stage XI?) and bred to G1 as claimed. Tables 1-4 do not teach otherwise. Furthermore, expression is also affected by positional effects upon integration of the retroviral vector, the amount of retroviral vector microinjected, and time; therefore, it is not readily apparent that the amounts of expression obtained by applicants are out of reach using the method described by Sang.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 3, 5, 6, 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over MacArthur (US Patent 6,825,396), Ivarie (US Patent 6,730,822), or Sang (U.S. Patent Application Publication 2005/0273872), in view of Powers (J. Immunological Methods, 2001, Vol. 251, pg 123-135).

MacArthur, Ivarie, and Sang taught transgenic avians expressing antibodies in the amounts in claim 1 (and 3) for reasons cited above in the anticipation rejections. MacArthur, Ivarie, and Sang did not teach the antibody was a scFv-Fc antibody.

However, such antibodies were known in the art as described by Powers.

Thus, it would have been obvious to those of ordinary skill in the art at the time of filing to make a transgenic avian expressing an antibody using the method of MacArthur, Ivarie, or Sang, wherein the transgenic avian expressed the scFv-Fc antibody taught by Powers. Those of ordinary skill would have been motivated to make any antibody (including the scFv-Fc antibody of Powers) in transgenic chickens eggs could increase production of proteins, i.e. be used as bioreactors.

The chicken of MacArthur, Ivarie or Sang combined with Powers inherently has the scFv-Fc content "not lower than 20 µg/ml in blood, not lower than 5 µg/ml in egg white, not lower than 1 µg in egg yolk" as in claim 31 because it was made using the method claimed (microinjecting at least 24 hours after the start of incubation) and has the same structure described by applicants as being part of the invention.

Thus, Applicants' claimed invention as a whole is *prima facie* obvious in the absence of evidence to the contrary.

Overall, the burden remains on the applicants to establish a patentable distinction between the claimed and referenced products. The method in which the transgenic chickens were produced as claimed does not distinguish them over the transgenic chickens known in the art at the time of filing. "Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 227 USPQ 964, 966 (Fed. Cir. 1985). See also MPEP §2113.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached at the office on Monday through Friday from 9:30 am to 6:00 pm at 571-272-0738.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It

also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Peter Paras, can be reached on 571-272-4517.

The official fax number for this Group is (571) 273-8300.

Michael C. Wilson

/Michael C. Wilson/
Primary Patent Examiner